

## **II. Non-Technical Abstract**

There are presently more than 40,000 new cases of melanoma in the U.S. per year with 7,300 melanoma-related deaths. Patients with stage III disease have at least a 50% chance of recurrence after surgical resection; patients with stage IV melanoma have a median survival of less than 1 year and most of these patients eventually die of melanoma. Standard therapy is dacarbazine chemotherapy, and while response rates range from 8-25%, there is little evidence that treatment improves survival. Combination chemotherapy and biochemotherapy regimens have been reported to induce higher response rates with the disadvantage of greater toxicity and, to date, there is no evidence that they result in improved survival. New approaches to the treatment of this disease are needed.

The purpose of this study is to see if we can safely immunize against melanoma. In particular, we are trying to immunize against gp75 (also known as TRP-1), a melanosomal protein involved in melanin synthesis and expressed by melanoma cells. We will also study whether the vaccine causes any side effects. We expect 24 patients to participate in this study. All of the patients on this study will receive vaccine, but groups of patients will receive increasing doses. Because of this, the first patients to be treated in this study will receive lower doses of the vaccine than the later patients, watching for side-effects to be sure that it is safe to give the higher doses. We believe, based on laboratory experiments, that the use of DNA vaccines could result in the production of immune substances (antibodies and T-cells) which recognize melanoma cells. The vaccine is a piece of DNA purified from bacteria which contains the gene for gp75. DNA is the blueprint that cells use to produce the substances that make up the body. The vaccine is made from DNA containing the code for gp75 from mice, which is very similar but not identical to human gp75 DNA.

Patients will be treated in the outpatient Clinical Immunology unit and will receive vaccinations into a muscle approximately every three weeks for the first 12 weeks of the study. The injections are given intramuscularly by a needleless device called a Bioject2000. This device is held in the hand and shoots the vaccine into the muscle. Blood will be drawn at regular intervals for analysis of antibodies. We will also be monitoring patients for any evidence of an effect on tumors.

## **III. Responses to Appendix M-II Through M-V**

### **Appendix M-II-A. OBJECTIVES AND RATIONALE FOR THE PROPOSED RESEARCH**

Please refer to the clinical protocol (IMCL CP09-0001), Section 1.0 'Introduction' and 2.0, 'Objectives'.